

WHAT IS CLAIMED IS:

1. An oligopeptide comprising an internalization sequence of at least about 8 amino acids and less than about 40 amino acids which has an amino acid sequence corresponding to the extracellular domain of a cell surface receptor;

5 wherein when combined with a cell expressing said cell surface receptor, said oligopeptide enhances the effect of ligand binding to said cell surface receptor.

2. An oligopeptide according to Claim 1, wherein oligopeptide has at least about 35% sequence similarity with the sequence of an α 1-domain of an MHC Class I antigen.

10 3. An oligopeptide according to Claim 2, wherein said sequence of an α 1-domain of an MHC Class I antigen is SEQ ID No:1.

15 4. An oligopeptide according to Claim 1, wherein said cell surface receptor is selected from the group consisting of insulin responsive glucose transporter, insulin receptor, leptin receptor, low density lipoprotein receptor, insulin like growth factor receptor, granulocyte colony stimulating factor receptor, interleukin 2 receptor, human growth hormone receptor and epidermal growth factor receptor.

5. An oligopeptide according to Claim 4, wherein said cell surface receptor is human.

6. An oligopeptide selected from the group consisting of SEQ ID NO:2; SEQ ID NO:3; SEQ ID NO:4; SEQ ID No:5; SEQ ID NO6; SEQ ID NO:7; SEQ ID NO:8; SEQ ID NO:9, and SEQ ID NO:12.

20 7. A method for inhibiting the internalization of a cell surface receptor response of a mammalian cell, said method comprising:

 adding to said mammalian cells an oligopeptide comprising an internalization sequence of at least about 8 amino acids and less than about 40 amino acids having an amino acid sequence corresponding to the extracellular domain of a cell surface
25 receptor;

wherein when combined with a cell expressing said cell surface receptor, said oligopeptide inhibits receptor internalization upon ligand binding.

8. A method according to Claim 7, wherein said oligopeptide has at least about 35% sequence similarity with the sequence of an α 1-domain of an MHC Class I antigen.

5 9. An oligopeptide according to Claim 8, wherein said sequence of an α 1-domain of an MHC Class I antigen is SEQ ID No:1.

10 10. A method according to Claim 7, wherein said cell surface receptor is selected from the group consisting of insulin responsive glucose transporter, insulin receptor, leptin receptor, low density lipoprotein receptor, insulin like growth factor receptor, granulocyte colony stimulating factor receptor, interleukin 2 receptor, human growth hormone receptor and epidermal growth factor receptor.

11. A method according to Claim 10, wherein said cell surface receptor is human.

15 12. A method according to Claim 10, wherein the sequence of said oligopeptide is selected from the group consisting of SEQ ID NO:2; SEQ ID NO:3; SEQ ID NO:4; SEQ ID NO:5; SEQ ID NO:6; SEQ ID NO:7; SEQ ID NO:8; SEQ ID NO:9, and SEQ ID NO:12.

20 13. A mammalian cell comprising a modified cell surface receptor, wherein said modification comprises an amino acid sequence substitution, insertion or deletion in an internalization sequence of the region of the extracellular domain, and wherein said modified sequence is of at least about 8 amino acids and less than about 40 amino acids;

wherein the ability of said cell surface receptor to internalize in response to ligand binding is altered by said modification.

25 14. A cell according to Claim 13, wherein said cell surface receptor is selected from the group consisting of insulin responsive glucose transporter, insulin receptor, leptin

receptor, low density lipoprotein receptor, insulin like growth factor receptor, granulocyte colony stimulating factor receptor, interleukin 2 receptor, human growth hormone receptor and epidermal growth factor receptor.

15. A cell according to Claim 14, wherein said cell surface receptor is human.

5 16. A cell according to Claim 11, wherein said modification comprises the deletion of a sequence selected from the group consisting of SEQ ID NO:2; SEQ ID NO:3; SEQ ID NO:4; SEQ ID NO:5; SEQ ID NO:6; SEQ ID NO:7; SEQ ID NO:8; SEQ ID NO:9 and SEQ ID NO:12.

10 17. A method of determining an internalization sequence of a cell surface receptor, said method comprising searching for a region of sequence similarity between said cell surface receptor and the sequence of an α 1-domain of an MHC Class I antigen, wherein the internalization sequence is involved in the internalization of said cell surface receptor.

15 18. A method according to Claim 17, wherein said oligopeptide has at least about 35% sequence similarity with the sequence of an α 1-domain of an MHC Class I antigen.

19. An oligopeptide according to Claim 18, wherein said sequence of an α 1-domain of an MHC Class I antigen is SEQ ID No:1.

20 20. A method for screening for an bioactive agent capable of modulating internalization of a cell surface receptor, said method comprising the steps of:
a) combining in a first sample a candidate bioactive agent with a cell according to Claim 13, in the presence of a ligand bound by said cell surface receptor;
b) combining in a second sample a candidate bioactive agent with a cell comprising said cell surface receptor in an unmodified form, in the presence of
25 a ligand bound by said cell surface receptor; and

c) determining the binding of said candidate agent to said first and said second samples;

wherein a change in binding of said agent in said second sample relative to said first sample indicates that said agent is capable of modulating internalization of said cell surface receptor.

21. A method for screening for a bioactive agent capable of modulating internalization of a cell surface receptor, said method comprising combining a cell surface receptor and a candidate bioactive agent, and determining the binding of said candidate agent to the the internalization sequence of said cell surface receptor.

22. A method according to claim 21, wherein said determination is done through competitive binding studies using a oligopeptide according to claim 1.

23. A method according to claim 22, wherein either the candidate bioactive agent or the oligopeptide is labelled.

24. A method according to claim 21, wherein said cell surface receptor comprises the full length cell surface receptor.

25. A method for screening for a bioactive agent capable of modulating internalization of a cell surface receptor, said method comprising the steps of:

a) combining

i) said cell surface receptor;

ii) a ligand bound by said cell surface receptor; and

iii) an oligopeptide according to claim 1, wherein said oligopeptide binds to the internalization sequence of said cell surface receptor;

to form a test mixture;

b) adding to said text mixture a candidate bioactive agent; and

c) determining the binding of said candidate bioactive agent to said internalization sequence;

wherein binding of said candidate bioactive agent to said internalization sequence indicates that said agent is capable of modulating internalization of said cell surface receptor.

26. A method according to claim 25 wherein said oligopeptide is labelled.

5 27. A method according to claim 25 wherein said candidate bioactive agent is labelled.

28. A method according to claim 25, wherein said cell surface receptor comprises the full length cell surface receptor.

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10 29. A method for screening for an bioactive agent capable of modulating internalization of a cell surface receptor, said method comprising the steps of:

- a) combining in a first sample said cell surface receptor, a ligand bound by said cell surface receptor, and an oligopeptide according to Claim 1;
- b) combining in a second sample a candidate bioactive agent, said cell surface receptor, a ligand bound by said cell surface receptor, and an oligopeptide
- 15 according to Claim 1; and
- c) determining the binding of said oligopeptide to said cell surface receptor in said first and said second samples;

wherein a change in binding of said oligopeptide in said second sample relative to said first sample indicates that said agent is capable of modulating internalization of said

20 cell surface receptor.

30. A method for screening for an bioactive agent capable of modulating internalization of a cell surface receptor, said method comprising the steps of:

- a) combining in a first sample a receptor-derived oligopeptide according to Claim 1, and a bioactive peptide having the sequence of an α 1-domain of an
- 25 MHC Class I antigen;

b) combining in a second sample a candidate bioactive agent, a receptor derived oligopeptide according to Claim 1, and a bioactive peptide having the sequence of an α 1-domain of an MHC Class I antigen; and

5 c) determining the association of said receptor-derived oligopeptide with said bioactive peptide having the sequence of an α 1-domain of an MHC Class I antigen in said first and said second samples;

wherein a change in said association in said second sample relative to said first sample indicates that said agent is capable of modulating internalization of said cell surface receptor.

10 31. A method according to Claim 22, wherein said sequence of an α 1-domain of an MHC Class I antigen is SEQ ID No:1.

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